General

Guideline Title

Guidelines on optimal feeding of low birth-weight infants in low- and-middle income countries.

Bibliographic Source(s)

World Health Organization (WHO). Guidelines on optimal feeding of low birth-weight infants in low- and middle-income countries. Geneva (Switzerland): World Health Organization (WHO); 2011. 51 p. [104 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Ratings schemes for the quality of evidence (high, moderate, low, very low) and the strength of the recommendations (strong, weak, situational) are defined at the end of the "Major Recommendations" field.

Number	Recommendation*	Type of Recommendation	Quality of Evidence (at least 1 critical outcome)
What to Feed?			
a. Choice of Milk			
1	Low-birth-weight (LBW) infants, including those with very low birth weight (VLBW), should be fed mother's own milk.	Strong	Moderate
2	LBW infants, including those with VLBW, who cannot be fed mother's own milk should be fed donor human milk (recommendation relevant for settings where safe and affordable milk-banking facilities are available or can be set up).	Strong situational	High
3	LBW infants, including those with VLBW, who cannot be fed mother's own milk or donor	Weak situational	Low

Number	Recommendation*	Type of Recommendation	Quality of Evidence (at least 1 critical outcome)
	human milk should be fed standard infant formula (recommendation relevant for resource-limited settings). VLBW infants who cannot be fed mother's own milk or donor human milk should be given preterm infant formula if they fail to gain weight despite adequate feeding with standard infant formula.		
4	LBW infants, including those with VLBW, who cannot be fed mother's own milk or donor human milk should be fed standard infant formula from the time of discharge until 6 months of age (recommendation relevant for resource-limited settings).	Weak situational	Low
5**	VLBW infants who are fed mother's own milk or donor human milk should not routinely be given bovine milk-based human-milk fortifier (recommendation relevant for resource-limited settings). VLBW infants who fail to gain weight despite adequate breast-milk feeding should be given human-milk fortifiers, preferably those that are human milk based.	Weak situational	Low
b. Supplements			
6**	VLBW infants should be given vitamin D supplements at a dose ranging from 400 i.u. to 1000 i.u. per day until 6 months of age.	Weak	Very low
7**	VLBW infants who are fed mother's own milk or donor human milk should be given daily calcium (120-140 mg/kg per day) and phosphorus (60-90 mg/kg per day) supplementation during the first months of life.	Weak	Low
8**	VLBW infants fed mother's own milk or donor human milk should be given 2-4 mg/kg per day iron supplementation starting at 2 weeks until 6 months of age.	Weak	Low
9	Daily oral vitamin A supplementation for LBW infants who are fed mother's own milk or donor human milk is not recommended at the present time, because there is not enough evidence of benefits to support such a recommendation.	Weak	Low
10	Routine zinc supplementation for LBW infants who are fed mother's own milk or donor human milk is not recommended at the present time, because there is not enough evidence of benefits to support such a recommendation.	Weak	Moderate
<u>When and How to Initiate Feeding?</u>			
11	LBW infants who are able to breastfeed should be put to the breast as soon as possible after birth when they are clinically stable.	Strong	Low
12**	VLBW infants should be given 10 ml/kg per day of enteral feeds, preferably expressed breast milk, starting from the first day of life, with the remaining fluid requirement met by intravenous fluids (recommendation relevant for resource-limited settings).	Weak situational	Low
<u>Optimal Duration of Exclusive Breastfeeding</u>			
13	LBW infants should be exclusively breastfed until 6 months of age.	Strong	Low
<u>How to Feed?</u>			
14	LBW infants who need to be fed by an alternative oral feeding method should be fed by cup (or palladai, which is a cup with a beak) or spoon.	Strong	Moderate
15**	VLBW infants requiring intragastric tube feeding should be given bolus intermittent feeds.	Weak	Low
16**	In VLBW infants who need to be given intragastric tube feeding, the intragastric tube may be placed either by oral or nasal route, depending upon the preferences of health-care providers.	Weak	Very low
<u>How Frequently to Feed and How to Increase the Daily Feed Volumes?</u>			

Number	Recommendation*	Type of Recommendation	Quality of Evidence (at least 1 critical outcome)
17	LBW infants who are fully or mostly fed by an alternative oral feeding method should be fed based on infants' hunger cues, except when the infant remains asleep beyond 3 hours since the last feed (recommendation relevant to settings with an adequate number of health-care providers).	Weak situational	Moderate
18**	In VLBW infants who need to be fed by an alternative oral feeding method or given intragastric tube feeds, feed volumes can be increased by up to 30 ml/kg per day with careful monitoring for feed intolerance.	Weak	Moderate

None of the recommendations address sick LBW infants and infants with birth weight less than 1.0 kg.

**These recommendations specifically address infants with birth weight between 1.0 and 1.5 kg.

Definitions:

Strength of the Recommendations

Each recommendation was graded as strong when there was confidence that the benefits clearly outweigh the harms, or weak when the benefits probably outweigh the harms, but there was uncertainty about the trade-offs. A strong or weak recommendation was further classified as situational if the benefits outweigh the harms in some situations but not in others. For example, some recommendations were considered relevant only to settings in low- and middle-income countries where resources were very limited while others were considered relevant only to settings where certain types of facilities were available.

Quality of the Evidence

High: One can be sure that the intervention is beneficial, has no effect or is harmful. The results, including the magnitude of the pooled effect, are unlikely to change with new studies.

Moderate: One can be reasonably sure that the intervention is beneficial, has no effect or is harmful. However, the magnitude of the pooled effect may change with new studies.

Low: Although it is likely that the intervention is beneficial, has no effect or is harmful, one cannot be sure. The magnitude of the pooled effect is uncertain and is likely to change with new studies.

Very low: One cannot be certain about the effects of the intervention.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Low birth weight (LBW) (<2.5 kg)
- Very low birth weight (VLBW) (1.0 to 1.5 kg)

Guideline Category

Management

Prevention

Clinical Specialty

Family Practice

Nutrition

Pediatrics

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To improve the quality of care received by low birth weight (LBW) infants in developing countries through improved capacity of health workers who care for these infants

Target Population

Clinically stable low birth weight (LBW)* infants in low- and middle-income countries, including infants born at term (after 37 and before 42 completed weeks of gestation) and preterm (born up to 37 completed weeks of gestation)

*Weighing between 1.0 and 2.5 kg at birth

Note: The recommendations do not specifically address the feeding of infants with a birth weight less than 1.0 kg (known as extremely LBW, ELBW), who are often clinically unstable and may require parenteral nutrition.

Interventions and Practices Considered

1. Choice of milk
    - Mother's own milk
    - Donor human milk
    - Standard infant formula
    - Preterm infant formula
    - Bovine milk-based human-milk fortifier
2. Supplements
    - Vitamin D
    - Calcium
    - Phosphorus

    - Iron
    - Vitamin A (not recommended routinely)
    - Zinc (not recommended routinely)
3. Initiation of breastfeeding as soon as possible after birth
4. Enteral feeds of expressed breast milk combined with intravenous fluids in very low birth weight (VLBW) infants
5. Exclusive breastfeeding for 6 months
6. Alternative oral feeding (cup, palladai, spoon)
7. Intragastric feeding in VLBW infants
8. Feeding volumes

Major Outcomes Considered

- Mortality
- Severe morbidity
- Neurodevelopment
- Anthropometric status

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Search Strategy

A series of systematic reviews were conducted and published by the World Health Organization (WHO) as *Optimal feeding of low-birth-weight infants: technical review* in 2006. The databases searched included the Cochrane Database of Systematic Reviews of randomized controlled trials (RCTs), the Cochrane Controlled Trials Register, the Cochrane Database of Abstracts of Reviews of Effectiveness (DARE), the Cochrane neonatal collaborative review group specialized register, MEDLINE (1966 to 2005), and EMBASE (1966 to 2005). The reference lists of relevant articles and a number of key journals were hand searched. Every effort was made to include relevant non-English language articles and abstracts. This approach was complemented by an additional search in August-September 2010 to identify relevant research papers published between January 2005 and August 2010. The first set of search terms ("all fields" and "MESH terms") was related to the population of interest: low-birth-weight (LBW) infant, preterm infant, premature infant, SGA infant, fetal growth retardation, intrauterine growth retardation, intrauterine growth restriction. The studies identified also needed to have at least one of the search terms in the second set related to issues in feeding of LBW infants. The second set of search terms included: feeding, enteral nutrition, breastfeeding, breast milk, human milk, donor milk, formula, human-milk fortifier, vitamin, micronutrient, vitamin A, vitamin D, calcium, phosphorus, zinc, iron, cup, bottle, spoon, tube, feeding tolerance, trophic feeding, minimal enteral nutrition and gut priming.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of the Evidence

A modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for assessing the quality of evidence was used. The quality of the set of included studies reporting results for an outcome was graded as: high, moderate, low or very low. The interpretation of the grades in these guidelines is:

High: One can be sure that the intervention is beneficial, has no effect or is harmful. The results, including the magnitude of the pooled effect, are unlikely to change with new studies.

Moderate: One can be reasonably sure that the intervention is beneficial, has no effect or is harmful. However, the magnitude of the pooled effect may change with new studies.

Low: Although it is likely that the intervention is beneficial, has no effect or is harmful, one cannot be sure. The magnitude of the pooled effect is uncertain and is likely to change with new studies.

Very low: One cannot be certain about the effects of the intervention.

The criteria used to grade the quality of evidence are shown in Table I of the original guideline document.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Abstraction and Summary Tables of Individual Studies

A standardized form was used to extract information from relevant studies. Systematically extracted data included: study identifiers, setting, design, participants, sample size, intervention or exposure, control or comparison group, outcome measures and results. The following quality characteristics were recorded for randomized controlled trials (RCTs): allocation concealment, blinding of intervention or observers, loss to follow-up, intention to treat analysis, analysis adjusted for cluster randomization (the latter only for cluster-RCTs). The quality characteristics recorded for observational studies were likelihood of reverse causality, selection bias and measurement bias, loss to follow-up and analysis adjusted for confounding.

The studies were stratified according to the type of intervention or exposure, study design, birth weight and gestational age, where possible. Effects were expressed as relative risks (RR) or odds ratios (OR) for categorical data, and as mean differences (MD) or weighted mean differences (WMD) for continuous data where possible. Where results adjusted for potential confounders were available, particularly for observational studies, they were used in preference to unadjusted results. Where results adjusted for potential confounders were not available, unadjusted results were used. All studies reporting on a critical outcome were summarized in a table of individual studies (see the Annexes in the original guideline document).

Pooled Effects

Pooled effects for developing recommendations were considered, wherever feasible. If results of three or more RCTs were available for an outcome, and the overall quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was at least "low", observational studies were not considered. However, if there were less than three RCTs for an outcome or the quality of evidence was "very low", the effects from RCTs were pooled with those from available cohort and case-control studies.

Pooled effects from published systematic reviews were used if the meta-analysis was appropriately done, and the reviews were up to date. However, if any relevant published study not included in the systematic review or a methodological problem with the meta-analysis was identified, the results were pooled using the "metan" command in Stata 11.0. For pooling, the author-reported adjusted effect sizes and confidence intervals (CIs) were used as far as possible. Random effects models for meta-analysis were used if there was important inconsistency in effects, and the random effects model was not unduly affected by small studies. Where pooling of results was not possible, the range of effect sizes observed in the individual studies was used in the development of recommendations.

Grading the Quality of Evidence

A modified GRADE approach for assessing the quality of evidence was used (see the "Rating Scheme for the Strength of the Evidence" field).

One of the difficulties in using GRADE is that the evidence base for an outcome may include studies with varying methodological quality and sample size. Therefore, the weight of the studies in the estimation of the pooled effect was included to make judgments about the quality of the set of included studies. The criteria used to grade the quality of evidence are shown in Table I in the original guideline document. The following briefly describes how these criteria were used:

Study Design

The included studies were classified as:

1. RCTs –including RCTs or cluster-RCTs
2. Non-randomized experimental studies
3. Observational studies, including cohort studies and case-control studies (studies with other observational designs were not included)

If a majority of evidence was from RCTs, indicated by over 50% weight in the pooled effect, a score of 0 was given. A score of -0.5 was given if a majority of evidence was from non-randomized experimental studies, and -1.0 if the evidence was from observational studies. See the original guideline document for the limitations and other details of these methods.

Methods Used to Formulate the Recommendations

Expert Consensus

Other

Description of Methods Used to Formulate the Recommendations

Formulation of Recommendations

The external guideline panel formulated the first version of the recommendations based on the technical review published in 2006. This version of guidelines was field tested in health facilities in four countries - Ghana, India, Pakistan and Uganda - in 2008-9.

After the evidence base was updated in 2010 and its quality graded using the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, the World Health Organization (WHO) staff prepared the second version of recommendations in a format consistent with the new WHO *Handbook for Guideline Development* (see the "Availability of Companion Documents" field).

The Guideline Development Group (GDG) met once to review the evidence synthesized in a technical review. The WHO working group and a consultant developed the draft guidelines based on this evidence. This draft was reviewed electronically by the GDG members and approved by them.

The GRADE system for grading recommendations was used. The strength of a recommendation reflects the degree of confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects. The decisions were made on the basis of evidence of benefits and harms, quality of evidence, values and preferences of policy-makers, health-care providers and parents, and whether costs are qualitatively justifiable compared to the benefits in low- and middle-income countries.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations

Each recommendation was graded as strong when there was confidence that the benefits clearly outweigh the harms, or weak when the benefits probably outweigh the harms, but there was uncertainty about the trade-offs. A strong or weak recommendation was further classified as situational if the benefits outweigh the harms in some situations but not in others. For example, some recommendations were considered relevant only to settings in low- and middle-income countries where resources were very limited while others were considered relevant only to settings where certain types of facilities were available.

Cost Analysis

A formal cost analysis was not performed; however, in making recommendations, guideline developers considered whether costs are qualitatively justifiable relative to benefits in low- and middle- income countries. Refer to the "Balance of benefits and harms, values and preferences, and costs" sections of the original guideline document for each recommendation.

Method of Guideline Validation

Clinical Validation-Trial Implementation Period

External Peer Review

Description of Method of Guideline Validation

The guideline was sent to the external expert panel for their review and inputs, which were incorporated into the final version of the guidelines.

Field Testing of Guidelines

Recommendations for feeding low-birth-weight (LBW) infants were first drafted in 2006, and a set of training materials for health workers who care for LBW infants was developed based on these recommendations. A field test with a pre-post design was conducted in two district-level hospitals each in Ghana, India, Pakistan and Uganda in 2008-9. The objectives of the field test were to evaluate the feasibility and acceptability of implementing the guidelines and to document the effect of guideline implementation on the knowledge and skills of health workers and mothers. The relatively small sample size of 120 infants per country was not sufficient to detect improvements in feeding practices.

In all countries, health providers who care for LBW infants were trained in a 3-day workshop comprised of self-reading sessions and classroom demonstrations using video and posters based on the guidelines, combined with clinical demonstrations and practice. A typical workshop included about 20 participants and 2-4 facilitators/trainers. In addition to training, supervision and on-the-job support was provided to the health workers, and efforts were made to improve facilities and supplies where possible.

The results of the field tests in all four countries were very encouraging. It was feasible to implement the guidelines in all the sites, and they were found to be acceptable to health workers and mothers. Both the health workers and mothers felt that implementation of the guidelines had improved the care of LBW infants. Finally, there was a substantial and statistically significant improvement in knowledge and skills of health providers related to optimal feeding of LBW infants in all the study sites.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Interventions to improve feeding are likely to improve the immediate and longer-term health and well-being of the individual infant and have a significant impact on neonatal and infant mortality at a population level.

Refer to the sections "Balance of benefits and harms, values and preferences, and costs" for each recommendation in the original guideline document for specific information.

Potential Harms

- Transmission of infections, such as human immunodeficiency virus (HIV), in human donor milk if safe milk-banking facilities are not available
- The possibility of harm in terms of increased risk of mortality and necrotizing enterocolitis (NEC) cannot be entirely ruled out in feeding multi-component fortified human milk.
- Contamination in the preparation of complementary foods in low- and middle-income country settings
- Nasogastric tube feeding has been associated with some deterioration in physiological parameters, such as airway resistance, and carries a risk of injury to the nasal mucosa.

Refer to the sections "Balance of benefits and harms, values and preferences, and costs" for each recommendation in the original guideline document for specific information.

Qualifying Statements

Qualifying Statements

- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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Implementation of the Guideline

Description of Implementation Strategy

These guidelines will be disseminated to Ministries of Health of relevant countries through the World Health Organization (WHO) Regional and Country offices. The draft training materials related to the guidelines, including the reading materials for sessions, posters and video, will be finalized and made available to countries through WHO Regional and Country Offices as reference material. However, the main implementation strategy for these guidelines and training materials will be through incorporation into the flagship tools and training materials of the Department of Maternal, Newborn, Child and Adolescent Health, including Integrated management of childhood illness (IMCI) and Integrated management of pregnancy and childbirth (IMPAC) materials for community, first-level health facilities and referral hospitals. These materials are already in use in over 100 countries.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). Guidelines on optimal feeding of low birth-weight infants in low- and middle-income countries. Geneva (Switzerland): World Health Organization (WHO); 2011. 51 p. [104 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

These guidelines were developed using funding to the Department of Maternal, Newborn, Child and Adolescent Health from the United States Agency for International Development.

Guideline Committee

Guideline Development Group

Composition of Group That Authored the Guideline

Guideline Development Group Members: Ramesh Agarwal, Zulfiqar Bhutta, Karen Edmond, Sandra Lang, Indira Narayanan, Samuel Newton, Vinod Paul, Muhammad Sohail Salat, María Asunción Silvestre, Nalini Singhal, Anthony Williams

WHO Staff Members: Rajiv Bahl, Carmen Casanovas, Bernadette Daelmans, Ornella Lincetto, Jeevasankar Mari, Jose Martines, Randa Saadeh

Consultants: Felicity Savage King participated in writing the draft guidelines; Peggy Henderson edited the final draft.

Financial Disclosures/Conflicts of Interest

None of the members of the Guideline Development Group (GDG) declared any conflicts of interest.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization Web site .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

Availability of Companion Documents

The following are available:

- A systematic review of HIV-free survival by feeding practices. From birth to 18 months. Geneva (Switzerland): World Health Organization (WHO); 2010 Jan 30. 23 p. Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization (WHO) Web site .
- WHO handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2008 Mar. 41 p. Electronic copies: Available in PDF from the WHO Web site .

An executive summary is available in the original guideline document .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 8, 2012.

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